

We claim:

1.

A genetically modified rodent all of whose cells comprise a Serca ATPase gene
5 modified by inserted recombination sites.

2.

The rodent of claim 1 comprising one or several copies of the modified Serca ATPase
gene.

10

3.

The rodent of claim 1, wherein the Serca ATPase gene is a Serca2 ATPase gene.

4.

15 The rodent of claim 1, wherein the recombination sites are of heterogenous origin.

5.

The rodent of claim 4, wherein the heterogenous recombination sites are of non-
mammalian origin.

20

6.

The rodent of claim 5, wherein the recombination sites comprise loxP recombination
sites.

25

7.

The rodent of claim 1 all of whose cells further comprise a gene encoding a
heterogenous recombinase.

8.

30 The rodent of claim 7, wherein the heterogenous recombinase is of non-mammalian
origin.

9.

The rodent of claim 8, wherein the recombinase is a Cre recombinase.

35

10.

The rodent of claim 7, wherein expression of the recombinase encoding gene is
controlled by a regulatory nucleic acid sequence.

11.

The rodent of claim 10, wherein the regulatory nucleic acid sequence is inducible.

5 12.

The rodent of claim 11, wherein said regulatory nucleic acid sequence is inducible by tamoxifen.

13.

10 The rodent of claim 7, wherein expression of the recombinase gene is tissue-specific.

14.

The rodent of claim 13, wherein expression of the recombinase gene occurs in heart tissue.

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15.

The rodent of claim 1, wherein the rodent is a mouse.

16.

20 A eukaryotic cell comprising a Serca ATPase gene modified by inserted recombination sites.

17.

25 The cell of claim 16 comprising one or several copies of the modified Serca ATPase gene.

18.

The cell of claim 16, wherein the Serca ATPase gene is a Serca2 ATPase gene.

30 19.

The cell of claim 16, wherein the recombination sites are of heterogenous origin.

20.

35 The cell of claim 19, wherein the heterogenous recombination sites are of non-mammalian origin.

21.

The cell of claim 20, wherein the recombination sites comprise loxP recombination sites.

5 22.

The cell of claim 16 further comprising a gene encoding a heterogenous recombinase.

23.

10 The cell of claim 22, wherein the heterogenous recombinase is of non-mammalian origin.

24.

The cell of claim 23, wherein the recombinase is a Cre recombinase.

15 25.

The cell of claim 22, wherein expression of the recombinase encoding gene is controlled by a regulatory nucleic acid sequence.

26.

20 The cell of claim 25, wherein the regulatory nucleic acid sequence is inducible.

27.

The cell of claim 16, wherein the cell is of mammalian origin.

25 28.

The cell of claim 27, wherein the cell is of non-human mammalian origin.

29.

The cell of claim 28, wherein the cell is of rodent origin.

30

30.

The cell of claim 29, wherein the cell is of mouse origin.

31.

35 The cell of anyone of claims 16-30, wherein said cell is an embryonic cell.

32.

The cell of anyone of claims 16-30, wherein said cell is a cardiomyocyte.

33.

A gene encoding a Serca ATPase modified by inserted recombination sites.

5 34.

The gene of claim 33, wherein the Serca ATPase is a Serca2 ATPase

35.

The gene of claim 33, wherein the recombination sites are of heterogenous origin.

10

36.

The gene of claim 35, wherein the heterogenous recombination sites are of non-mammalian origin.

15 37.

The gene of claim 36, wherein the recombination sites comprise loxP recombination sites.

38.

20 The gene of claims 34, wherein said gene is substantially modified as set forth in SEQ ID 1.

39.

A vector comprising the gene of claim 33.

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40

The vector of claim 39, wherein the vector is based on pBluescript II KS.

41.

30 A method for inducing defective Ca^{2+} handling in a non-human vertebrate, comprising the steps of inducing recombination and inactivation of a Serca ATPase gene.

42.

The method of claim 41, wherein the Serca ATPase gene is a Serca2 ATPase gene.

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43.

The method of claim 41, wherein the Serca gene is inactivated in heart tissue.

44.

The method of claim 41, wherein said non-human vertebrate is the rodent of anyone of claims 7, 8, 9, 10, 11, 12, or 13.

5 45.

A method for inducing heart failure in non-human vertebrate, comprising the steps of inducing recombination and inactivation of a Serca ATPase gene in heart tissue.

46.

10 The method of claim 45, wherein the Serca ATPase gene is a Serca2 ATPase gene.

47.

The method of claim 45, wherein said vertebrate is the rodent of claim 14.

15

48.

A method for screening a compound or a mixture of compounds for activity against defective Ca^{2+} handling, comprising the steps of inducing recombination and inactivation of a Serca ATPase gene in a non-human vertebrate; administering the
20 compound or mixture to said mammal before and/or after the induced inactivation of the Serca ATPase gene.

49.

The method of claim 48, wherein the Serca ATPase gene is a Serca2 ATPase gene.

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50.

The method of claim 48, wherein the Serca gene is inactivated in heart tissue.

51.

30 The method of claim 48, wherein said vertebrate is the rodent of anyone of claims 7, 8, 9, 10, 11, 12, or 13.

52.

A method for screening a compound or a mixture of compounds for activity against
35 heart failure, comprising the steps of inducing recombination and inactivation of a Serca ATPase gene in heart tissue of a non-human vertebrate; administering the compound or mixture to said mammal before and/or after the induced inactivation of the Serca ATPase gene.

53.

The method of claim 52, wherein the Serca ATPase gene is a Serca2 ATPase gene.

5 54.

The method of claim 52, wherein said vertebrate is the rodent of claim 14.